REMARKS

Claims 1-24 are pending in the instant application. Claim 1 has been amended to clarify the claimed invention. In particular, claim 1 has been amended to recite "*placental* stem cell" and "*mammalian* placenta"; to recite that perfusion solution is used in "an amount sufficient" to flush out "a detectable amount of placental" stem cells; and to rearrange existing limitations for better clarity. Claims 2-24 have been canceled, without prejudice to Applicant's right to resubmit and prosecute these claims in a related application. New claims 25-46 have been added. Support for the amendments to claim 1, and for new claims 25-46, can be found in the specification of the application, as outlined in the following table:

CLAIM(S)	SUPPORT IN SPECIFICATION
1	Page 1, ¶ 2; page 4 "Draining of Cord Blood and Storage of Fresh Placenta"; pages 4-5 "Extraction of Cells"; page 11, last ¶ to page 12, first ¶; Fig. 4
25	Page 2- page 3, first ¶; page 4 "Draining of Cord Blood and Storage of Fresh Placenta"; pages 4-5 "Extraction of Cells"; Example 1; FIG. 4
26	Page 6, ¶ 2; page 10, last ¶ to page 12, first ¶
27	Page 6, ¶ 2; page 10, last ¶
28	Page 4, last ¶
29	Page 5, last ¶; page 9, second ¶
30	Page 5, last ¶; page 9, second ¶
31	Page 5, last ¶; page 9, second ¶
32	Page 5, first ¶; page 9, last ¶
33	Page 5, first ¶; page 9, last ¶ to page 10, first ¶
34	Page 5, first ¶, last ¶; page 9, last ¶ to page 10, first ¶
35	Page 5, first ¶, last ¶; page 9, last ¶ to page 10, first ¶
36	Page 6, ¶ 2; page 10, last ¶ to page 12, first ¶
37	Page 6, ¶ 2; page 10, last ¶ to page 12, first ¶
38	Page 5, last ¶
39	Page 5, last ¶

40	Page 4, ¶¶ 1, 2
41	Page 4, ¶¶ 1, 2
42	Page 4, ¶¶ 1, 2
43	Page 5, last ¶
44	Page 7, ¶ 2
45	Page 7, ¶ 2
46	Page 4, first ¶; page 8, last ¶ to page 9, ¶ 2

No new matter has been added.

Upon entry of the amendments made herein, claims 1 and 25-46 will be pending in the present application.

CLAIM OBJECTIONS

The Examiner has objected to claims 7, 9, 10 and 12 because the Examiner contends that the preamble and method steps of the claims do not correlate. According to the Examiner, these claims "are drawn to a method of producing new cells and bioactive molecules in the perfused placenta, yet . . . depend from a method for collecting embryonic-like stem cells from un-perfused placenta." Office Action at page 2. Claims 1 and 6, from which claims 7, 9, 10 and 12 depend, quite clearly recite that the placenta *is*, in fact, perfused. Nevertheless, Applicant has canceled claims 7, 9, 10 and 12, mooting this rejection.

THE REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

The Examiner has rejected claims 7 and 10-24 under 35 U.S.C. § 112, first paragraph, as nonenabled. Applicant has canceled claims 7 and 10-24, mooting this rejection.

With respect to claims 7 and 10, the Examiner appears to contend that the invention as claimed is not enabled because "the specification is silent regarding the cells [that] remain in the placenta and their state or differentiation, and thus, fails to teach what type of new cells could be produced." Office Action at page 3. In support of this contention, the Examiner cites Ma *et al.*, *Tissue Engineering* 5:91-102 (1999) ("Ma") for the proposition that "the outermost layer of chorionic villi is trophoblast cells, and they are terminally differentiated and lasting no more than about seven days . . ." Office action at page 3. The Examiner also cites Contractor *et al.*, *Cell. Tiss. Res.* 237:609-617 (1984) ("Contractor") for the proposition that "even under nutritional perfusion, oedema and microvillous damage appeared after *three hours* of placental perfusion." Office Action at pages 3-4 (emphasis in original). Thus, the

Examiner argues nonenablement based upon the apparent lifetime of certain cells within the placenta.

The references cited by the Examiner do not support a nonenablement argument. Amended claim 1 and the new claims are directed to a method of collecting placental *stem cells*, which are not terminally differentiated, and have an indefinite lifespan. Thus, the teaching of Ma *et al.* is not relevant to amended claim 1, or to the new claims. Likewise, Contractor not only uses a significantly different perfusion procedure than used in the instant method (*see* Contractor, pages 610-612), but fails to discuss any effect that such perfusion procedures may have on placental stem cells. Instead, Contractor focuses on apparent damage to specific cell types, such as syncytiotrophoblasts, cytotrophoblasts and epithelial cells. Contractor, therefore, does not demonstrate that the methods of the present invention would not work as described. In fact, using the methods disclosed in the present application, one may obtain placental stem cells from placentas maintained, and perfused, for 24 hours or more. Thus, the method of collecting placental stem cells, as currently claimed, is fully enabled.

THE REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

The Examiner has rejected claims 1-24 under 35 U.S.C. § 112, second paragraph, as indefinite in the recitation of "embryonic like stem cells." The Examiner contends that the specification does not define this term, and thus the metes and bounds of the claims are unclear. The Examiner has interpreted the term to include hematopoietic stem cells. Applicant disagrees that the claims are indefinite, for the following reasons.

Applicant points out that, on page 1, the specification states: "The present invention is generally in the area of stem cell collection, and particularly in the recovery of embryonic-like stem cells . . . *from placentas*. These embryonic-like stem cells *are derived from the placenta* . . ." Page 1, ¶ 2. Thus, the specification clearly defines the placenta itself as the source of these stem cells. Moreover, the specification differentiates hematopoietic stem cells from placental stem cells. *See, e.g.*, page 2, ¶¶ 2 and 4. To clarify that the placenta provides these stem cells, Applicant has amended claim 1 to recite "placental stem cell" rather than "embryonic-like stem cell." New claims 25-46, which depend ultimately from claim 1, are similarly directed to methods of collecting placental stem cells. The claims, therefore, do not encompass a method of collecting hematopoietic stem cells, as the Examiner contends. New claims 25-46, which depend ultimately from claim 1, are similarly directed to a method using a mammalian placenta. Finally, Applicant has canceled claims 2-24, mooting

the rejection of these claims on this basis. Applicant therefore respectfully requests that the Examiner withdraw the rejection of the claims on this basis.

The Examiner has also rejected claims 1-24 as indefinite because of the claim limitations "collecting embryonic-like stem cells from a placenta" or "propagating exogenous cells in a placental bioreactor," because "placenta" and "placental" encompass plant structures. Applicant submits that no one of skill in the art would interpret "placenta" in the context of the claims as pending as including plant structures, because the claims, and the specification, require that the placenta be drained of *cord blood*. No plant on earth contains cord blood. The recited placenta, of course, is derived from a mammal. To clarify this, Applicant has amended claim 1 to recite this inherent feature of the invention. Finally, Applicant has canceled claims 2-24, mooting the rejection of these claims on this basis.

The Examiner has rejected claims 6, and claims 7 and 10, as lacking sufficient antecedent basis in the recitation of "said additional anticoagulant perfusion solution" and "said newly produced cells," respectively. Applicant has canceled claims 6, 7 and 10, mooting the rejection of these claims on this basis.

The Examiner has rejected claim 11 as indefinite because of the recitation of "the cells in the placenta," because the phrase could refer to cells from cord blood or from the placenta itself. Applicant has canceled claim 11, mooting the rejection of this claim on this basis.

Finally, the Examiner has rejected claims 11 and 12 as indefinite in the recitation of "the cells in the placenta are genetically engineered with exogenous DNA." Applicant has canceled claims 11 and 12, mooting the rejection of these claims on this basis.

THE REJECTIONS UNDER 35 U.S.C. § 103(a)

The Examiner has rejected claims 1-6, 8 and 11 under 35 U.S.C. § 103(a) as being unpatentable over Boyse *et al.*, U.S. Patent No. 6,461,645 in view of Belvedere *et al.*, *Stem Cells* 18;245-51 (2000), Sanders *et al.*, U.S. Patent No. 3,862,002 and Addison *et al.*, *J. Steroid Biochem. Mol. Biol.* 39(1):83-90 (1991). Moreover, the Examiner has rejected claims 1-6, 8, 9 and 11 over the above combination, further in view of Bersinger *et al.*, *Reprod. Fertil. Devel.* 4:585-88 (1992). Applicant submits that the cited combination of references fails to render the claims obvious, as explained below.

The initial burden is on the Examiner to make out a *prima facie* case of obviousness. MANUAL OF PATENT EXAMINING PROCEDURE (MPEP) § 2142, at 2100-96. To establish a *prima facie* case of obviousness, three criteria must be met. First, there must be some

suggestion or motivation, either in the references themselves or in the knowledge available to one of skill in the art to combine the references. Second, there must be a reasonable expectation of success. Finally, the prior art references, when combined, must teach or suggest all of the claim limitations. MPEP § 2142, at 2100-97.

First, Applicants have canceled claims 2-6, 8, 9 and 11; thus, the rejection of these claims on this basis is moot.

Second, the references were combined pursuant to a flawed assumption. The Examiner has assumed that "embryonic like stem cells," recited in claim 1, includes hematopoietic stem cells. Office Action, page 10. This is not the case, as the specification defines "embryonic like stem cells" as stem cells that are derived from the *placenta*, not from cord blood, and differentiates these stem cells from stem cells derived from cord blood. *See* Application, page 1, ¶ 2; and page 2, ¶¶ 2 and 4. Applicant has amended claim 1 to clarify that the stem cells recited in claim 1 are *placental* in origin; the newly-added claims reflect this terminology as well. Moreover, the specification teaches that cord blood is *removed* prior to perfusion with the anticoagulant solution used to collect the placental stem cells. This aspect of the claimed invention is present in both the claims as currently pending, and as will be pending upon entry of the present Amendment. Thus, the method as claimed excludes hematopoietic stem cells.

Given this exclusion, the combination of references fails to teach every element of the claims because it fails to teach or suggest the collection of placental stem cells, or non-cord blood-derived stem cells. Boyse, the main reference cited by the Examiner, does not teach the collection of placental stem cells. Instead, as the Examiner has indicated, Boyse teaches only the collection of hematopoietic stem cells, Office Action, page 12, and these cells are collected only from blood.

The secondary references cited by the Examiner also fail to teach or suggest the collection of placental stem cells. For example, Belvedere *et al.* teaches only a method of extracting additional amounts of cord blood from a placenta and the characterization of hematopoietic cell populations found therein; this reference fails to teach the collection or characterization of placental-derived stem cells. Sanders teaches only a system for producing physiologically active placental substances using viable placental tissue. Sanders, as the Examiner notes, fails to teach, or even hint at the possibility of, the collection of hematopoietic stem cells, or any other stem cell types, from the perfusate surrounding the placental tissue. Office Action, page 13. Addison, as the Examiner points out, fails to teach obtaining hematopoietic stem cells, or any other type of stem cell. Office Action, page 13.

Thus, the combination of references cited by the Examiner fails to teach this critical limitation of the claims.

Moreover, the combination of references fails to teach that perfusion, as required by claim 1, is a means of obtaining stem cells. Sanders, Addison and Bersinger teach perfusion only in the context of characterizing substances, such as hormones, present in the perfusate. These references absolutely fail to teach that perfusion is a method for collecting *cells*. Conversely, Boyse and Belvedere teach only that cells may be collected from cord blood, and then only by gravity drainage, needle aspiration, or pressure. Nothing in any of the references suggests that perfusion may be used to collect placental-derived stem cells. A person of skill in the art, therefore, would *not* have combined the cited references to arrive at the claimed invention. Indeed, persons of skill at the art would not, in any case, have used Boyse and Belvedere, which teach only hematopoietic stem cell collection from cord blood, to arrive at the invention of claim 1, which specifically recites *removal* of cord blood prior to collection of stem cells.

Thus, because the combination of references fails to teach all limitations of the claims, both as currently pending, and as will be pending upon entry of the present Amendment, and because a person of skill in the art would not be motivated to combine the references, the combination cannot render the claims of the instant application obvious. Applicant therefore respectfully requests that the Examiner withdraw the rejection of the claims on this basis.

THE OBVIOUSNESS-TYPE DOUBLE PATENTING REJECTIONS

The Examiner has provisionally rejected claim 1 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 16 and 17 of copending application no. 10/074,976 ("the '976 application"). The Examiner states that "the claims of the present application and that of the cited patent application are each drawn to a method comprising the steps of exsanguinating and perfusing the placenta, and *collecting embryonic-like stem cells from said placenta*." Office Action at page 16 (emphasis added). Applicants request that the Examiner hold this rejection in abeyance until such time as relevant claims of the '976 application, or the instant application, are allowed.

The Examiner has also provisionally rejected claims 1, 6 and 8 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 27-33 of the '180 application. Applicants submit that this rejection is now inappropriate for two reasons.

First, Applicant, on June 5, 2003, filed with the Patent and Trademark Office a Response to Restriction Requirement for the '180 application in which Applicant elected to prosecute claims 1-18 and 54, drawn to an isolated mammalian placenta. Thus, claims 27-33 of the '180 application, on which the Examiner bases the provisional obviousness-type double patenting rejection, are no longer pending, and the basis for the rejection no longer exists. Second, Applicant has canceled claims 6 and 8, rendering the provisional rejection of these claims moot. Applicant therefore respectfully requests that the Examiner withdraw the provisional rejection of the claims on this basis.

CONCLUSION

Applicants respectfully request consideration of the foregoing remarks and entry of the foregoing amendments into the file of the above-identified application. Applicants believe that each ground for rejection has been successfully overcome or obviated, and that all the pending claims are in condition for allowance. Withdrawal of the Examiner's rejections and allowance of the application are respectfully requested.

Respectfully submitted,

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